510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K050394

B. Purpose for Submission:

New 510(k)

C. Measurand:

Amphetamines (d-Amphetamine)
Benzodiazepines (Nordiazepam)
Cocaine (Benzoylecgonine)
Methamphetamine (d-Methamphetamine)
Methadone (Methadone)
Opiates (Codeine/Morphine)
Phencyclidine (Phencyclidine)
Cannabinoids (11-nor-9-carboxy-Δ9-THC)

D. Type of Test:

Qualitative visually read immunochromatographic test for drugs in urine

E. Applicant:

Medtox Diagnostics, Inc.

F. Proprietary and Established Names:

Sure-Screen

G. Regulatory Information:

1. Regulation section:
   862.3100, Enzyme Immunoassay, Amphetamine
   862.3170, Enzyme Immunoassay, Benzodiazepine
   862.3870, Enzyme Immunoassay, Cannabinoids
   862.3250, Enzyme Immunoassay, Cocaine and Cocaine Metabolites
   862.3620, Enzyme Immunoassay, Methadone
   862.3610, Thin Layer Chromatography, Methamphetamine
   862.3650, Enzyme Immunoassay, Opiates
   862.3100, Enzyme Immunoassay, Amphetamine - Phencyclidine

2. Classification:

   Class II

3. Product code:
   DKZ, JXM, LDJ, DIO, DJR, DJC, DJG, LCM, respectively

4. Panel:

   91 (Toxicology)

H. Intended Use:

1. Intended use(s):

   See indications for use.

2. Indication(s) for use:
   The SURE-SCREEN Drugs of Abuse Test System uses immunochromatographic test strips for the rapid, qualitative detection of one or more of the following: Amphetamines, Benzodiazepines, Cocaine, Methamphetamine, Methadone, Opiates, Phencyclidine and THC (Cannabinoids) in human urine. It is intended for prescription point-of-care use including workplace settings, criminal justice or forensic settings, drug rehabilitation clinics, physician offices and laboratory settings. SURE-SCREEN is not for over-the-counter sale.

   Operators that may use this device are defined as individuals with a minimum of a high school education with no formal laboratory training or experience. Individuals should also satisfy the following training and certification guidelines: (1)Training should be conducted by a qualified professional and include a demonstration of the SURE-SCREEN test system and (2) the use of quality assurance samples for monitoring and confirming the performance of the test system. Trainers should observe and confirm that the operator (3) uses proper technique when running a test sample and quality assurance samples, (4) has a basic understanding of test results, including a the potential for false positive and false negative results, (5) knows how to prepare a sample for shipment to the laboratory for confirmation testing, (6) has reviewed the information contained in the MEDTOX SURE-SCREEN Training and Certification Program (available at www.medtox.com and that the operator (7) minimally achieves a score of 80% on the written exam provided by MEDTOX .

   Operators achieving a score of 80% will be provided with a certificate of training participation. Quality assurance samples appropriate for training are available from MEDTOX Laboratories Inc. Additionally, MEDTOX Technical Support will provide access to assistance from individuals who are experienced in the

interpretation of drug testing results.

Sure-Screen detects drug classes at the following cutoff concentrations:

(AMP) Amphetamines (d-Amphetamine)	300 ng/mL
(BZO) Benzodiazepines (Nordiazepam)	200 ng/mL
(COC) Cocaine (Benzoylecgonine)	100 ng/mL
(MAMP) Methamphetamine (d-Methamphetamine)	300 ng/mL
(MTD) Methadone (Methadone)	200 ng/mL
(OPI) Opiates (Morphine)	100 ng/mL
(PCP) Phencyclidine (Phencyclidine)	25 ng/mL
(THC) Cannabinoids (11-nor-9-carboxy-Δ^9-THC)	40 ng/mL

Many of the cutoff concentrations for these tests are below those recommended by SAMHSA. Additionally, many of these tests are positive at levels significantly below the claimed cutoff concentration. The rate of false positive results with tests having sensitivities this low has not been studied. However, the rate of false positives generally increases as the cutoff concentration of the test is lowered. See the Precision/Sensitivity section for more information.

The SURE-SCREEN drugs of abuse test system provides only a preliminary analytical test result. A more specific alternate chemical method must be used in order to obtain a confirmed analytical result. Gas chromatography/mass spectrometry (GC/MS) or liquid chromatography/tandem mass spectrometry (LC/MS/MS) is the preferred confirmatory method. Clinical consideration and professional judgment should be applied to any drug of abuse test result.

It is the responsibility of those organizations required to follow Department of Transportation (DOT) or Substance Abuse Mental Health Services Administration (SAMHSA) Workplace Drug Testing Guidelines to determine that use of this product satisfies the criteria for workplace testing established under DOT and SAMHSA authority.

3. Special conditions for use statement(s):

   The device is for in vitro diagnostic prescription use.

4. Special instrument requirements:
   Not applicable. The device is a visually read single-use device.

I. Device Description:

The device consists of a single-use test cup with a specialized lid. The lid contains individual test strips for each of the drugs being tested. When the cup is tipped, the urine comes into contact with the bottom of each test strip, thereby initiating the

reaction. Users determine the result by visually determining the presence or absence of a line. Each strip includes an internal process control.

This device is a one-step immunochromatographic test intended for the detection of amphetamines, benzodiazepines, cocaine, methamphetamine/MDMA, methadone, opiates, phencyclidine and cannabinoids in human urine. The principle of the test relies upon the competitive binding of unbound drug and drug bound to protein (applied as a test line on the nitrocellulose) with the specific antibody (absorbed to colloidal gold) targeted to the drug.

The device includes adulteration checks, the Lateral Flow Adulterant Strip, or LFAS. There is also a temperature check on the cup. Because these are not medical devices, they are not included in the review and do not appear in the indications for use.

The sponsor indicates the test does not contain any human source material.

The training guide and certification, including a 17 question quiz is included with the submission.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   PROFILE II and PROFILE-ER

2. Predicate 510(k) number(s):

   k982211 and k002331

3. Comparison with predicate:
   Both devices are qualitative immunochromatographic visually read single-use tests for measurement of the same analyte(s) in the same matrix. Both are competitive immunoassays.

   The cutoff concentrations vary, with the candidate device having lower cutoffs in all but one of the assays, i.e., PCP. The candidate device has also been modified to a cup-type configuration.

K. Standard/Guidance Document Referenced (if applicable):
The sponsor did not reference any guidance documents or standards.

L. Test Principle:

Each test strip contains antibody colloidal gold, a drug conjugate and a control line. Mouse monoclonal antibodies are mixed with colloidal gold and applied to the sample well pads of the strip. Drug is conjugated to protein and immobilized at the test line. Strips have an anti-mouse immunoglobulin antibody immobilized at the control line. The anti-mouse antibody binds the mouse antibodies coated on the colloidal gold.

When the test cup is tipped over, urine flows into the sample well of the device, the dried antibody-colloidal gold on the sample pad dissolves and the urine wicks up the white test strips carrying the red antibody-colloidal gold with it.

Interpretation of Results

Negative: When no drug is present in the urine sample, the red antibody-colloidal gold migrates up the test strip and binds to the drug conjugate immobilized on the membrane. The binding of the antibody-colloidal gold to the drug conjugate generates a line at the test line.

Non-negative: When a drug is present in the sample the antibody-colloidal gold binds the drug before it migrates up the test strip. However, when the antibody-colloidal gold binds the drug in the urine, the antibody-colloidal gold can not bind to the drug conjugate immobilized on the test strip. When the drug concentrating is at or above the cutoff concentration, the majority of the antibody colloidal gold is bound to the drug from the urine. Therefore, as drug bound antibody-colloidal gold migrates up the test strip it is unable to bind to the drug conjugate immobilized on the membrane. Therefore no line is generated at the "T" location on the device.

Control Line: Each test strip has an internal procedural control. A control line forms when the antibody-colloidal gold binds to the anti-mouse immunoglobulin antibody immobilized on the membrane at the "C" location on the device. A line must form at the control "C" location on the device to indicate that there was an adequate volume of sample, the reagents migrated properly, and that the test strip is intact.

M. Performance Characteristics (if/when applicable):

1. <u>Analytical performance:</u>

   a. Precision/Reproducibility:

   Performance around the cutoff concentration for each drug was evaluated by testing drug-free urines spiked with standard solutions. Drug-free urines were also tested. Testing was performed in triplicate on 5 different occasions by 3 Medtox employees. Results were read at five minutes.

   Data from this study is pooled and presented, below. There were significant differences between results read by different operators. However, most often this

occurred below the claimed cutoff concentration, and may not be as significant. Many positive results are observed significantly below the cutoff concentration. There are also negative results occurring at and above the cutoff. The sponsor has no explanation for these inconsistencies other than operator error.

Amphetamine (d-Amphetamine) Cutoff = 300 ng/mL			
Conc. (ng/mL)	Number Tested	Positive	Negative
0	540	0	540
75	45	0	45
150	45	13	32
225	45	38	7
300	45	44	1
375	45	44	1
450	45	44	1

Benzodiazepines (Nordiazepam) Cutoff = 200 ng/mL			
Conc. (ng/mL)	Number Tested	Positive	Negative
Negative	540	0	540
50	45	30	15
100	45	40	5
150	45	45	0
200	45	45	0
250	45	44	1
300	45	45	0

Cocaine (Benzoylecgonine) Cutoff = 100 ng/mL			
Conc. (ng/mL)	Number Tested	Positive	Negative
Negative	540	0	540
25	45	0	45
50	45	19	26
75	45	25	20
100	45	35	10
125	45	44	1
150	45	41	4

Methamphetamine (d-Methamphetamine) Cutoff = 300 ng/mL			
Conc. (ng/mL)	Number Tested	Positive	Negative
Negative	540	0	540
75	45	1	44
150	45	18	27
225	45	44	1
300	45	45	0
375	45	45	0

450	45	45	0

Methadone (Methadone) Cutoff = 200 ng/mL			
Conc. (ng/mL)	Number Tested	Positive	Negative
Negative	405	0	405
50	45	4	41
100	45	37	8
150	45	44	1
200	45	45	0
250	45	44	1
300	45	45	0

Opiate (Morphine) Cutoff = 100 ng/mL			
Conc. (ng/mL)	Number Tested	Positive	Negative
Negative	540	0	540
25	45	20	25
50	45	38	7
75	45	44	1
100	45	45	0
125	45	44	1
150	45	43	2

Phencyclidine (Phencyclidine) Cutoff = 25 ng/mL			
Conc. (ng/mL)	Number Tested	Positive	Negative
Negative	540	0	540
6.25	45	1	44
12.50	45	0	45
18.75	45	17	28
25.00	45	43	2
31.25	45	43	2
37.50	45	44	1

Cannabinoids (11-nor-9-carboxy-Δ^9-THC) Cutoff = 40 ng/mL			
Conc. (ng/mL)	Number Tested	Positive	Negative
Negative	105	0	105
10	45	0	45
20	45	0	45
30	45	1	44
40	45	45	0
50	45	40	5

60	45	45	0

POC Studies

Precision studies were performed by 3 POC operators. Operators were trained and educated in a similar manner to those participating in the method comparison study. Samples were drug-free urines, the majority of which were spiked with multiple drugs to concentrations that were 25% above the cutoff, at the cutoff, 50% below the cutoff, and 75% below the cutoff concentrations. Results appear below.

Amphetamine (d-Amphetamine) Cutoff = 300 ng/mL			
Conc. (ng/mL)	Number Tested	Positive	Negative
Negative	135	0	135
75	45	4	41
150	45	35	10
300	45	45	0
375	45	45	0

Benzodiazepines (Nordiazepam) Cutoff = 200 ng/mL			
Conc. (ng/mL)	Number Tested	Positive	Negative
Negative	135	0	135
50	45	1	44
100	45	4	41
200	45	9	36
250	45	45	0

Cocaine (Benzoylecgonine) Cutoff = 100 ng/mL			
Conc. (ng/mL)	Number Tested	Positive	Negative
Negative	135	0	135
25	45	0	45
50	45	6	39
100	45	26	19
125	45	45	0

Methamphetamine (d-Methamphetamine) Cutoff = 300 ng/mL			
Conc. (ng/mL)	Number Tested	Positive	Negative
Negative	135	0	135
75	45	1	44
150	45	11	34
300	45	25	20
375	45	45	0

Methadone (Methadone) Cutoff = 200 ng/mL			
Conc. (ng/mL)	Number Tested	Positive	Negative
Negative	135	0	135
50	45	4	41
100	45	22	23
200	45	25	20
250	45	45	0

Opiate (Morphine) Cutoff = 100 ng/mL			
Conc. (ng/mL)	Number Tested	Positive	Negative
Negative	135	0	135
25	45	0	45
50	45	0	45
100	45	7	38
125	45	43	2

Phencyclidine (Phencyclidine) Cutoff = 25 ng/mL			
Conc. (ng/mL)	Number Tested	Positive	Negative
Negative	135	0	135
6.25	45	1	44
12.5	45	34	11
25.0	45	44	1
31.25	45	45	0

Cannabinoids (11-nor-9-carboxy-Δ^9-THC) Cutoff = 40 ng/mL			
Conc. (ng/mL)	Number Tested	Positive	Negative
Negative	135	0	135
10	45	2	43
20	45	14	31
40	45	25	20
50	45	45	0

Results are similar in this POC study to those observed in the professional study.

b. Linearity/assay reportable range:

Not applicable. The assay is intended for qualitative use.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

The sponsor did not indicate any degree of traceability for their devices.

Control materials are required but are not specifically identified in the labeling.

No calibrators are required. The device is calibrated during the manufacturing process.

Product Stability:
Stability studies depend on readouts from an instrument (BioDot). The BioDot reader takes a picture of a test line, and converts it to a number which is proportional to the line intensity. Readings less that 0.6 are typically read as positive (absence of a line) and those above 1.1 are typically read as negative (a line is present). Those between 0.6 and 1.1 are visually interpreted as borderline results. The sponsor provided the following in support of these conclusions.

Artificial Test Strips were used to simulate lines on a test strip. Numerous Test Strips were read by 29 operators. The BioDot range of readings are compared to the visual observations of the readers.

Data to Support Equivalence Between BioDot Readings and Visually Read Results

BioDot Range	Positive Results Read Visually	Negative Results Read Visually	Rate
≥ 2.0	19	3287	99% Negative
1.1-1.9	75	389	83% Negative
0.7- 1.0	156	163	51% Negative
≤ 0.6	423	12	97% positive

Stability Protocol:
Drug tests are stored at 2 - 8°C and room temperature.
Drug tests are assayed at 3, 6, 12, 18 and 25 months intervals.
Twenty samples are run on each of three different lots of each of each drug test.
The twenty replicates consist of the following:

- 5 replicates of a positive urine (containing drug at a concentration of 50% above the cutoff)
- 15 replicates of a drug-free urine

Readings are recorded and averaged for each lot.

Acceptance Criteria for the Study:
Drug-free urine should have a BioDot reading of 2.5 reading or greater.
Individual test line intensities should be 2.0 or greater.
Urine spiked with drug 50% above the cutoff should have an average BioDot test line intensity of 0.6 or less. Individual test line intensities

should be 0.8 or less.

Calculations used to estimate shelf life are:
At 20K Cal/mole; 12 months (365 days) at 25° C is equivalent to 44 days at 45°C; 15 months at 25° C is equivalent to 55 days at 45°C. 24 months at 25°C is equivalent to 88 days at 45°C.

Users are instructed to follow federal, state, and local guidelines concerning QC practices.

d. Detection limit:

Sensitivity of qualitative assays may be characterized by validating performance around the claimed cutoff concentration of the assay, and demonstrating the lowest concentration of drug that is capable of or consistently producing a positive result. This information appears in the precision section, above.

Most tests render positive results well below the claimed cutoff concentration.

e. Analytical specificity:

Cross-Reactivity

The following metabolites and compounds were initially dissolved in appropriate solvents and then added at varying concentrations to drug-free urine for evaluation. Samples were evaluated in triplicate by in-house operators. Results are expressed as the minimum concentration of metabolite or compound required to produce a positive test result. Percent cross reactivity of a compound is calculated by dividing the cutoff concentration by the minimum concentration required to obtain a positive result and then multiplying by 100%.

Amphetamine (d-amphetamine, cutoff = 300 ng/mL)	**Result** Positive at 300 ng/mL	**% Cross-Reactivity** 100%
l-Amphetamine	Positive at 100,000 ng/mL	< 1%
Ephedrine	Negative at 100,000 ng/mL	< 1%
MDA	Positive at 750 ng/mL	40%
MDE (MDEA)	Negative at 100,000 ng/mL	< 1%
MDMA	Negative at 100,000 ng/mL	< 1%
d-Methamphetamine	Negative at 100,000 ng/mL	< 1%
l-Methamphetamine	Negative at 100,000 ng/mL	< 1%
Phenethylamine	Negative at 100,000 ng/mL	< 1%
Phentermine	Positive at 1,000 ng/mL	33%
Tyramine	Negative at 100,000 ng/mL	< 1%

Benzodiazepines (Nordiazepam, cutoff = 200 ng/mL)	**Result** Positive at 200 ng/mL	**% Cross-Reactivity** 100%
Alprazolam	Positive at 25 ng/mL	800%
Alprazolam, 1-Hydroxy	Positive at 500 ng/mL	40%
7-Amino-clonazepam	Negative at 100,000 ng/mL	< 1%
7-Amino-flunitrazepam	Negative at 100,000 ng/mL	< 1%
Chlordiazepoxide	Negative at 100,000 ng/mL	< 1%
Clobazam	Positive at 25 ng/mL	800%
Clonazepam	Positive at 125 ng/mL	160%
Clorazepate	Positive at 50 ng/mL	400%
Desalkylflurazepam	Positive at 100 ng/mL	200%
Desmethyl-chlordiazepoxide	Positive at 250 ng/mL	80%
Desmethylflunitrazepam	Positive at 50 ng/mL	400%
Diazepam	Positive at 50 ng/mL	400%
Flunitrazepam	Positive at 50 ng/mL	400%
Flurazepam	Negative at 100,000 ng/mL	< 1%
Lorazepam	Positive at 2500 ng/mL	8%
Lorazepam glucuronide	Positive at 25 ng/mL	800%
Lysergic acid	Positive at 25,000 ng/mL	< 1%
Midazolam	Negative at 100,000 ng/mL	< 1%.
Nitrazepam	Positive at 50 ng/mL	400%
Oxazepam	Positive at 25 ng/mL	800%
Oxazepam glucuronide	Positive at 750 ng/mL	27%
Pyrilamine	Positive at 10,000 ng/mL	2%
Sidenfil	Positive at 10,000 ng/mL	2%
Sulindac	Positive at 10,000 ng/mL	2%
Temazepam	Positive at 50 ng/mL	400%
Temazepam glucuronide	Positive at 250 ng/mL	80%
Triazolam	Positive at 75 ng/mL	267%
Triazolam, 1-hydroxy	Negative at 10,000 ng/mL	< 1%

Cocaine (Benzoylecgonine, cutoff = 100 ng/mL)	**Result** Positive at 100 ng/mL	**% Cross-Reactivity** 100%
Cocaine	Positive at 300 ng/mL	33%
Ecgonine	Positive at 100,000 ng/mL	< 1%
Ecgonine Methyl Ester	Negative at 100,000 ng/mL	< 1%

Methamphetamine (d-Methamphetamine, cutoff = 300 ng/mL)	**Result** Positive at 300 ng/mL	**% Cross-Reactivity** 100%

d-Amphetamine	Positive at 75,000 ng/mL	< 1%
l-Amphetamine	Negative at 100,000 ng/mL	< 1%
Ephedrine	Positive at 75,000 ng/mL	< 1%
Fenfluramine	Positive at 10,000 ng/mL	3%
MDA	Negative at 100,000 ng/mL	< 1%
MDE (MDEA)	Positive at 25,000 ng/mL	1.2%
MDMA	Positive at 1000 ng/mL	33%
l-Methamphetamine	Positive at 2500 ng/mL	12%
Methcathinone	Positive at 25,000 ng/mL	1.2%

Methadone (Methadone, cutoff = 200 ng/mL)	**Result** Positive at 200 ng/mL	**% Cross-Reactivity** 100%
EDDP	Negative at 100,000 ng/mL	< 1%
EMDP	Negative at 100,000 ng/mL	< 1%

Opiates (Morphine, cutoff = 100 ng/mL)	**Result** Positive at 100 ng/mL	**% Cross-Reactivity** 100%
Apomorphine	Negative at 100,000 ng/mL	< 1%
Codeine	Positive at 300 ng/mL	33%
Diacetylmorphine	Positive at 300 ng/mL	33%
Dihydrocodeine	Positive at 100 ng/mL	100%
Ethylmorphine	Positive at 50 ng/mL	200%
Hydrocodone	Positive at 300 ng/mL	33%
Hydromorphone	Positive at 100 ng/mL	100%
Levorphanol	Positive at 50,000 ng/mL	< 1%
Lidocaine	Negative at 100,000 ng/mL	< 1%
6-Monoacetylmorphine	Positive at 100,000 ng/mL	< 1%
Morphine 3-β-D-Glucuronide	Positive at 100,000 ng/mL	< 1%
Morphine 6-β-D-Glucuronide	Negative at 100,000 ng/mL	< 1%
Nalorphine	Positive 150 ng/mL	67%
Naloxone	Positive at 25,000 ng/mL	< 1%
Naltrexone	Negative at 100,000 ng/mL	< 1%
Norcodeine	Negative at 100,000 ng/mL	< 1%
Oxycodone	Positive at 50,000 ng/mL	< 1%
Oxymorphone	Positive at 75,000 ng/mL	< 1%
Procaine	Negative at 100,000 ng/mL	< 1%
Thebaine	Positive at 1,000 ng/mL	10%

Phencyclidine (Phencyclidine, cutoff = 25	**Result** Positive at 25 ng/mL	**% Cross-Reactivity** 100%

ng/mL)		
4-Hydroxy-Phencyclidine	Positive at 5,000 ng/mL	<1%

THC (Cannabinoids) (11-nor-9-carboxy-Δ^9-THC, cutoff = 40 ng/mL)	**Result** Positive at 40 ng/mL	**% Cross-Reactivity** 100%
Cannabidiol	Negative at 100,000 ng/mL	< 1%
Cannabinol	Negative at 100,000 ng/mL	< 1%
l-11-Hydroxy- Δ^9-THC	Positive at 250 ng/mL	16%
Δ^9-Tetrahydrocannabinol	Positive at 10,000 ng/mL	< 1%
Δ^8-Tetrahydrocannabinol (Δ^6-Tetrahydrocannabinol)	Positive at 25,000 ng/mL	< 1%

Non Cross-reactive Endogenous Compounds

Listed compounds were initially dissolved in appropriate solvents and then added to drug-free urine for evaluation with all eight Sure-Screen tests. Most of the compounds were evaluated for reactivity with the Sure-Screen tests at 100 µg/mL (albumin was evaluated at 20 mg/mL and bilirubin was evaluated at 200 µg/mL). Samples were evaluated in triplicate by in-house operators. The listed compounds gave negative results with all eight of the Sure-Screen tests.

Acetaldehyde	Creatinine	Hemoglobin, Human
Acetone	Epinephrine	Sodium Chloride
Albumin, Human	β-Estradiol	Tetrahydrocortisone
Bilirubin	Estriol	d,1-Thyroxine
Cholesterol	Glucose Std. Solution	Uric Acid

Unrelated Compounds, Prescription and Over-the-Counter Medications

An extensive list of compounds were dissolved in solvents and added to drug-free urine for evaluation with all eight Sure-Screen tests. Most of the compounds were evaluated for reactivity at 100 µg/mL. Samples were evaluated in triplicate by in-house operators and the list of compounds evaluated appears in the package insert. Compounds that demonstrated reactivity are listed, below.

Phenelzine-mAMP
Pyrilamine-BZO
Selegiline (Deprenyl)-mAMP
Sildenafil (Viagra)-BZO

Interference

pH and Specific Gravity:

All tests were assayed with six negative clinical samples with pH values of 4.0, 5.0, 6.0, 7.0, 8.0 and 9.0 ± 0.1. Each sample was assayed in triplicate. All results were negative. The affects of these conditions on samples containing drug is not known.

Similarly, all tests were assayed with drug-free urines with specific gravity values of 1.003, 1.005, 1.011, 1.016, 1.019, 1025 and 1.033. Each sample was assayed in triplicate. All samples were negative. The affects of these conditions on samples containing drug is not known.

Common Drugs:
Drug free urine samples were spiked with the Sure-Screen targeted drugs to the concentrations of 25% and 150% of the cutoff concentrations. 100 µg/mL of the common drugs listed below, were then added to the preparation and assayed. Evaluations were performed in triplicate by in-house operators. None of the common drugs listed in the following table affected the expected results.

COMMON DRUGS EVALUATED WITH ALL SURE-SCREEN TESTS

Acetylsalicylic Acid	Chlorpheniramine	Ibuprofen
Acetaminophen	Cocaine-COC	Morphine-OPI
Brompheniramine maleate	Doxylamine	Phenobarbital
Caffeine	Dextromethorphan	d-Pseudoephedrine
Carbamazepine	Diphenylhydantoin	Salicylic Acid

There is the possibility that other substances and/or factors not listed above may interfere with the test and cause false results, e.g., technical or procedural errors.

f. Assay cut-off:

The PCP cutoff concentration is consistent with the cutoff currently recommended by SAMHSA. However, the cutoff concentrations for amphetamines, cocaine, methamphetamines, opiates, and THC are below those recommended by SAMHSA. There are currently no recommendations for the rest of the tests.

There has been no evaluation of false positive rates using these cutoff concentrations. The sponsor has, however, included the following information in their package insert:

A positive test result does not always mean a person took illegal drugs and a negative test result does not always mean a person did not take illegal drugs. There are a number of factors that influence the reliability of drug tests. Certain drug of abuse tests are more accurate than others.

<u>For Preliminary Positive Tests</u>: In general, the Substance Abuse and Mental Health Services Administration (SAMHSA) reports the accuracy of drug tests as[a]:

60 out of 100 times a "preliminary positive" result from an opiate test is a "false preliminary positive" result. This means that the result of the first test was "preliminary positive" even though the person did not take an illegal drug.
50 out of 100 times a "preliminary positive" test result from an amphetamine or methamphetamine test is a "false preliminary positive" result.
50 out of 100 times a "preliminary positive" result from a PCP (phencyclidine) test is a "false preliminary positive" result.
10 out of 100 times a "preliminary positive" result from a marijuana test is a "false preliminary positive" result.
2 out of 100 times a "preliminary positive" result from a cocaine test is a "false preliminary positive" result.

[a] *Data was generated from laboratory tests that have the following cutoff concentrations: Marijuana, 50 ng/mL; Cocaine, 300 ng/mL; Phencyclidine, 25 ng/mL; Opiates, 2000 ng/mL; Amphetamines, 1000 ng/mL. In general, the rates of false preliminary positive results will increase as the cutoff concentration of the test is lowered.*

Characterization of how the device performs analytically around the claimed cutoff concentration appears in the precision section (M,1, a), above.

2. Comparison studies:

a. Method comparison studies:

Performance was evaluated by assaying a panel of blind coded clinical urine samples containing varying concentrations of drugs with Sure-Screen. Results were then compared to GC/MS or LC/MS/MS results. Samples were obtained from MEDTOX Laboratories. There were screened using a commercial immunoassay having traditional cutoff concentrations, i.e., significantly higher than Sure-Screen cutoff concentrations (except for PCP). Samples with negative results by both the commercial immunoassay system and Sure-Screen were not confirmed. Samples with positive results by either the commercial immunoassay system or Sure-Screen were confirmed by GC/MS or LC/MS/MS. Most samples were unaltered clinical samples, however, to include samples with concentrations close to the cutoff 6 BZO samples were diluted with negative urine. Testing was performed by MEDTOX personnel. Readings were taken at 5 minutes.

Amphetamine

Confirmatory Result	Negative by immunoassay, or if positive, no drug present (above the limit of detection of the confirmatory method)	Concentration range of up to 50% below the cutoff (ng/mL)	Concentration range between the -50% of the cutoff and the cutoff (ng/mL)	Concentration range between the cutoff and 50% above the cutoff (ng/mL)	Concentration range of greater than 50% above the cutoff (ng/mL)

Range of sample concentrations			180 – 255	334 – 402	474 – 11845
Positive	0	No samples analyzed in this range	4	4	32
Negative	55	No samples analyzed in this range	1	1	1

Samples are categorized according to d-amphetamine concentrations.

Benzodiazepines

Confirmatory Results	Negative by immunoassay used to screen the samples, or if positive, no drug present (above the limit of detection of the confirmatory method	Concentration range of up to 50% below the cutoff (ng/mL)	Concentration range between the -50% of the cutoff and the cutoff (ng/mL)	Concentration range between the cutoff and 50% above the cutoff (ng/mL)	Concentration range of greater than 50% above the cutoff (ng/mL)
Concentration Range			113 - 151	220 – 281	428 - 12491
Positive	0	No samples analyzed in this range	4	5	33
Negative	54	No samples analyzed in this range	0	0	0

Nordiazepam, oxazepam, temazepam, alprazolam and α-hydroxy-alprazolam were added together to determine the total benzodiazepine concentration reported in the table. 6 samples were diluted with negative urine to obtain concentrations around the cutoff.

Cocaine

Confirmatory Result	Negative by immunoassay, or, if positive, no drug present (above the limit of detection of the confirmatory method)	Concentration range of up to 50% below the cutoff (ng/mL)	Concentration range between the -50% of the cutoff and the cutoff (ng/mL)	Concentration range between the cutoff and 50% above the cutoff (ng/mL)	Concentration range of greater than 50% above the cutoff (ng/mL)

Concentration Range			55 – 91	110 - 140	153 - 96924
Positive	0	No samples analyzed in this range	6	5	36
Negative	54	No samples analyzed in this range	0	0	0

Samples are categorized by benzoylecgonine concentrations (cocaine metabolite).

Methamphetamine

Confirmatory Results	Negative by immunoassay used to screen the samples, or if positive, no drug present (above the limit of detection of the confirmatory method	Concentration range of up to 50% below the cutoff (ng/mL)	Concentration range between the -50% of the cutoff and the cutoff (ng/mL)	Concentration range between the cutoff and 50% above the cutoff (ng/mL)	Concentration range of greater than 50% above the cutoff (ng/mL)
		62 – 88	156 – 248	318 – 429	479 – 1499
Positive	2	0	5	6	51
Negative	98	2	0	0	0

Samples are categorized according to d-methamphetamine concentrations

Methadone

Confirmatory Results	Negative by immunoassay used to screen the samples, or if positive, no drug present (above the limit of detection of the confirmatory method	Concentration range of up to 50% below the cutoff (ng/mL)	Concentration range between the -50% of the cutoff and the cutoff (ng/mL)	Concentration range between the cutoff and 50% above the cutoff (ng/mL)	Concentration range of greater than 50% above the cutoff (ng/mL)
Concentration Range			112 - 114	249 - 283	307 - 9411
Positive	0	No samples analyzed in this range	2	6	44
Negative	98	No samples analyzed in this range	2	1	0

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Opiates

Confirmatory Results	Negative by immunoassay, or if positive, contains no drug (above the limit of detection of the confirmatory method	Concentration range of up to 50% below the cutoff (ng/mL)	Concentration range between the -50% of the cutoff and the cutoff (ng/mL)	Concentration range between the cutoff and 50% above the cutoff (ng/mL)	Concentration range of greater than 50% above the cutoff (ng/mL)
Concentration Range			76 – 90	111 – 147	251 – 136360
Positive	0	No samples analyzed in this range	4	4	36
Negative	54	No samples analyzed in this range	0	0	0

Morphine, codeine, hydrocodone and hydromorphone were added together to determine the total opiate concentrations reported in this table.

Phencyclidine

Confirmatory Results	Negative by immunoassay used to screen the samples, or if positive, contained no drug (above the limit of detection of the confirmatory method	Concentration range of up to 50% below the cutoff (ng/mL)	Concentration range between the -50% of the cutoff and the cutoff (ng/mL)	Concentration range between the cutoff and 50% above the cutoff (ng/mL)	Concentration range of greater than 50% above the cutoff (ng/mL)
Concentration Range			13 - 22	27 – 35	39 - 5439
Positive	0	No samples analyzed in this range	2	5	33
Negative	55	No samples analyzed in this range	3	0	0

Cannabinoid

Confirmatory Results	Negative by immunoassay used to screen the samples, or if positive, contained no drug (above the	Concentration range of up to 50% below the cutoff	Concentration range between the -50% of the cutoff and the cutoff	Concentration range between the cutoff and 50% above the cutoff (ng/mL)	Concentration range of greater than 50% above the cutoff (ng/mL)

	limit of detection of the confirmatory method	(ng/mL)	(ng/mL)		
Concentration Range		3	21 - 37	42 – 54	62 - 761
Positive	0	0	5	8	34
Negative	55	1	1	0	0

11-nor-9-carboxy-Δ^9-THC concentrations are reported in this table

POC Studies

Performance was also evaluated by 13 POC staff at 44 POC locations. Operators ran 1000 blinded samples obtained from MEDTOX Laboratories. Sure-Screen test results were compared to GC/MS or LC/MS/MS results. Operators were provided with instructions from the package insert. Almost all operators had no formal laboratory training, but 88% of the operators had run point-of-care testing devices prior to this study. 26/44 operators had greater than a high school education.

Samples were selected similarly to how samples were selected for the in-house study, however this study included a high number of negative samples, and a much lower percentage of positive samples, i.e., a total of 4 or 6 samples. Many studies included few, if any, samples that were challenging to the cutoff concentration of the assay. Samples with negative results by both the commercial immunoassay system and Sure-Screen were not confirmed. Samples with positive results by either the commercial immunoassay system or Sure-Screen were confirmed by GC/MS or LC/MS/MS.

The number of POC facilities and operators

Facility Type	Criminal Justice	Treatment Center	Clinic/Physician Office Laboratory	DAU Collection Site	Total
Sites	2	2	7	2	13
Operators	18	3	11	12	44
Samples	375	75	250	300	1000

Sure-Screen results compared to confirmatory results are presented, below.

Amphetamine

Confirmatory Results	Negative by immunoassay used to screen the samples, or if positive, contained no drug (above the limit of detection of the	Concentration range of up to 50% below the cutoff	Concentration range between the -50% of the cutoff and the cutoff (ng/mL)	Concentration range between the cutoff and 50% above the cutoff	Concentration range of greater than 50% above the cutoff (ng/mL)

	confirmatory method	(ng/mL)		(ng/mL)	
Concentration Range		119	217-257	306	510-9489
Positive	6	0	4	1	21
Negative	967	1	0	0	0

Samples are categorized according to d-amphetamine concentrations.

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Benzodiazephines

Confirmatory Results	Negative by immunoassay used to screen the samples, or if positive, contained no drug (above the limit of detection of the confirmatory method	Concentration range of up to 50% below the cutoff (ng/mL)	Concentration range between the -50% of the cutoff and the cutoff (ng/mL)	Concentration range between the cutoff and 50% above the cutoff (ng/mL)	Concentration range of greater than 50% above the cutoff (ng/mL)
Concentration Range		34-38	113-174	245-268	315-32454
Positive	0	1	5	2	17
Negative	971	1	2	0	0

Nordiazepam, oxazepam, temazepam, alprazolam and α-hydroxy-alprazolam were added together in an unweighted fashion to determine the total benzodiazepine concentration reported in the table.

Cocaine

Confirmatory Results	Negative by immunoassay used to screen the samples, or if positive, contained no drug (above the limit of detection of the confirmatory method	Concentration range of up to 50% below the cutoff (ng/mL)	Concentration range between the -50% of the cutoff and the cutoff (ng/mL)	Concentration range between the cutoff and 50% above the cutoff (ng/mL)	Concentration range of greater than 50% above the cutoff (ng/mL)
Concentration Range		16-48	57-96	113-133	200-39644
Positive	1	1	4	5	28
Negative	959	2	0	0	0

Samples are categorized by benzoylecgonine concentrations (cocaine metabolite).

Methamphetamine

Confirmatory Results	Negative by immunoassay used to screen the samples, or if positive, contained no drug (above the limit of detection of the confirmatory method	Concen-tration range of up to 50% below the cutoff (ng/mL)	Concentration range between the -50% of the cutoff and the cutoff (ng/mL)	Concentration range between the cutoff and 50% above the cutoff (ng/mL)	Concentration range of greater than 50% above the cutoff (ng/mL)
Concentration Range			217	403	564-10585
Positive	8	No samples analyzed in this range	1	1	14
Negative	976	No samples analyzed in this range	0	0	0

Samples are categorized according to d-methamphetamine concentrations.

Methadone

Confirmatory Results	Negative by immunoassay used to screen the samples, or if positive, contained no drug (above the limit of detection of the confirmatory method	Concentration range of up to 50% below the cutoff (ng/mL)	Concentration range between the -50% of the cutoff and the cutoff (ng/mL)	Concentration range between the cutoff and 50% above the cutoff (ng/mL)	Concentration range of greater than 50% above the cutoff (ng/mL)
Concentration Range				207	335-8377
Positive	0	No samples analyzed in this range	No samples analyzed in this range	1	6
Negative	993	No samples analyzed in this range	No samples analyzed in this range	0	0

Opiates

Confirmatory Results	Negative by immunoassay used to screen the samples, or if positive, contained no drug (above the limit of detection of the confirmatory method	Concentration range of up to 50% below the cutoff (ng/mL)	Concentration range between the -50% of the cutoff and the cutoff (ng/mL)	Concentration range between the cutoff and 50% above the cutoff (ng/mL)	Concentration range of greater than 50% above the cutoff (ng/mL)
Concentration Range		28	60	124-143	241-11724
Positive	8	1	1	2	25
Negative	963	0	0	0	0

Morphine, codeine, hydrocodone and hydromorphone were added together in an unweighted fashion to determine the total opiate concentrations reported in this table.

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PCP

Confirmatory Results	Negative by immunoassay used to screen the samples, or if positive, contained no drug (above the limit of detection of the confirmatory method	Concentration range of up to 50% below the cutoff (ng/mL)	Concentration range between the -50% of the cutoff and the cutoff (ng/mL)	Concentration range between the cutoff and 50% above the cutoff (ng/mL)	Concentration range of greater than 50% above the cutoff (ng/mL)
Concentration Range					236-373
Positive	0	No samples analyzed in this range	No samples analyzed in this range	No samples analyzed in this range	4
Negative	996	No samples analyzed in this range	No samples analyzed in this range	No samples analyzed in this range	0

Cannabinoid

Confirmatory Results	Negative by immunoassay used to screen the samples, or if positive, contained no drug (above the limit of detection of	Concentration range of up to 50% below the cutoff (ng/mL)	Concentration range between the -50% of the cutoff and the cutoff (ng/mL)	Concentration range between the cutoff and 50% above the cutoff (ng/mL)	Concentration range of greater than 50% above the cutoff (ng/mL)

	the confirmatory method				
Concentration Range		5-17	23-26	47-59	60-481
Positive	8	4	3	6	30
Negative	946	3	0	0	0

11-nor-9-carboxy-Δ^9-THC concentrations are reported in this table.

.b. Matrix comparison:

Not applicable. The assay is intended for only one sample matrix.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable. Clinical studies are not typically submitted for this device type and matrix.

b. Clinical specificity:

Not applicable. Clinical studies are not typically submitted for this device type and matrix. The specificity is likely to be less than traditional assays, however, as the cutoff concentrations are significantly lower.

c. Other clinical supportive data (when a. and b. are not applicable):

4. Clinical cut-off:

Validation of the clinical appropriateness of the cutoff is not typically submitted for this device type and matrix.

5. Expected values/Reference range:
No elicit drugs should be present in urine. Legitimate over-the-counter and prescription drugs may cause positive results.

N. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

The device also includes tests for detected adulteration of the sample. Because these products are not medical devices, aspects related to this claim were not reviewed. References to the adulteration checks are therefore not included in the intended use statement, but appear in the package insert.

O. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

P. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.